BC Centre for Palliative Care

# B.C. INTER-PROFESSIONAL PALLIATIVE SYMPTOM MANAGEMENT GUIDELINES



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# HICCOUGHS

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## DEFINITION

Hiccoughs are repeated, involuntary spasmodic contractions of the diaphragm and inspiratory muscles followed by sudden closure of the glottis.[1-7] Hiccoughs are categorized according to duration[2,3,4,5,8,9]:

**Acute** – Hiccoughs that last < 48 hours and are common, non-pathologic, and self-limited.[10]

**Persistent** - Hiccoughs lasting 2 days or more.

**Intractable** – Hiccoughs that last more than 1 month and not responsive to treatments.

## PREVALENCE

Persistent or intractable hiccoughs often indicate serious underlying pathology and are most common (10-20%)[4] in those with gastro-intestinal tract, thoracic, or central nervous system disease.[3,5,9-11] Prevalence is relatively low (~1-9%) in the general palliative population.[2,9,12-18]

## IMPACT

Persistent and intractable hiccoughs can interfere with normal daily activity,[5,19] significantly reducing quality of life, causing distress for both patient and family.[4] Potential impacts include: increased anxiety, distress,[7] insomnia, fatigue,[5,20] gastrointestinal reflux, weight loss, vomiting, aspiration pneumonia, dehydration, electrolyte imbalance, cardiac arrhythmias,[21-25] isolation, delirium (in the elderly), wound dehiscence (in post-surgery),[3,9] depression, and in rare situations, death.[23,26-30]

## STANDARD OF CARE

### Step 1 | Goals of care conversation

Determine goals of care in conversation with the patient, family and inter-disciplinary team. Refer to additional resources (Additional resources for management of hiccoughs) for tools to guide conversations and required documentation. Goals of care may change over time and need to be reconsidered at times of transition, e.g., disease progression or transfer to another care setting.

## Step 2 | Assessment

### Hiccough Assessment: Using Mnemonic O, P, Q, R, S, T, U and V[71]

| **Mnemonic Letter** | **Assessment Questions** *Whenever possible, ask the patient directly. Involve family as appropriate and desired by the patient.* |
|---|---|
| **Onset** | When did the hiccoughs begin? How long do they last? How often do they occur? |
| **Provoking /Palliating** | What brings them on? What makes them better? What makes them worse? |
| **Quality** | What do they feel like? Can you describe them? Do they change when you change position? |
| **Region/Radiation** | Not applicable |
| **Severity** | How severe is this symptom? What would you rate it on a scale of 0-10 (0 being none and 10 being the worst possible)? Right now? At worst? On average? How bothered are you by this symptom? Are there any other symptom(s) that accompany this symptom (e.g., nausea, anxiety or fatigue)? |
| **Treatment** | What medications and treatments are you currently using? Are you using any non-prescription treatments, herbal remedies, or traditional healing practices? How effective are these? Do you have any side effects from the medications and treatments? What have you tried in the past? Do you have concerns about side effects or cost of treatments? |
| **Understanding** | Do they interfere with your ability to eat, drink, talk or enjoy other activities? Do they interfere with your sleep? What do you believe is causing this symptom? How are the hiccoughs affecting you and/or your family? What is most concerning to you? |
| **Values** | What overall goals do we need to keep in mind as we manage this symptom? What is your acceptable level for this symptom (0-10)? Are there any beliefs, views or feelings about this symptom that are important to you and your family? |

**Symptom Assessment:** Physical assessment as appropriate for symptom

**Diagnostics:** consider goals of care before ordering diagnostic testing

Recognize that hiccoughs can be multifactorial in advanced disease and that an extensive workup to find the cause can be harmful. Consider patient status and goals of care in determining extent of diagnostics required.[8]

- Perform a detailed history and physical.[4, 9]
- Review prior surgical interventions; respiratory and gastrointestinal symptoms; infections; and use of alcohol and medications, especially corticosteroids, benzodiazepines, and barbiturates.[18]
- Consider CBC, electrolytes, and chest xray.[9] Include liver ultrasound and liver function tests, serum Calcium,[10, 26, 31] CT, MRI and electrocardiography, as needed.[4]
- Invasive tests such as lumbar puncture and bronchoscopy, depend on the patient's situation.[26]

## Step 3 | Determine possible causes and reverse as possible if in keeping with goals of care (For more details, see Underlying causes of hiccoughs in palliative care)

Over 100 underlying diseases have been associated with hiccoughs.[1,31] Persistent hiccoughs should be taken seriously as they often indicate underlying pathology.

### Common causes of persistent and intractable hiccoughs include[1,2,4,32,33]

- Gastric stasis and distention (most common)[34]
- Gastro-esophageal reflux[34]
- Metabolic disturbances (e.g., uremia, hypercalcemia, low magnesium)[15]
- Infection
- Irritation of the diaphragm or phrenic nerve

*Step 3 - Determine possible causes continued on* next page

### Determine possible causes and reverse as possible if in keeping with goals of care *continued*

- Hepatobiliary disease/hepatomegaly
- Cerebral causes (e.g., tumour, metastasis, CVD)[8]

### Other important causes

- Myocardial Infarction, pericarditis, aneurysm.[2,7,8,35]
- Medications such as benzodiazepines, opioids, corticosteroids.[2] Risk with dexamethasone is 25%.[15,19] (See Underlying causes of hiccoughs in palliative care for a list of medication causes)
- Chemotherapy, radiotherapy, and surgery[15,18,26,37-39]; nasal, pharyngeal, laryngeal conditions; foreign body in ear canal.[2]
- Anxiety, stress or over-excitement; psychogenic.[2,7]

## PRINCIPLES OF MANAGEMENT

When considering a management approach, always balance burden of a possible intervention against the likely benefit (e.g., does the intervention require transfer to another care setting?).

- Hiccoughs may resolve on their own; try simple physical techniques.
- Try non-pharmacological interventions during acute 48 hours “bout” phase, particularly any that the patient has previously found helpful.
- Consider medications when they are persistent, lasting more than 48 hours.
- Consider the patient’s general condition to avoid potential side effects.[8]
- Refer to palliative care consultants when refractory or patient unable to swallow.

## LEGEND FOR USE OF BULLETS

Bullets are used to identify the type or strength of recommendation that is being made, based on a review of available evidence, using a modified GRADE process.

| | |
|---|---|
| ✓ | **Use with confidence:** recommendations are supported by moderate to high levels of empirical evidence. |
| ⬟ | **Use if benefits outweigh potential harm:** recommendations are supported by clinical practice experience, anecdotal, observational or case study evidence providing low level empirical evidence. |
| ⚠ | **Use with caution:** Evidence for recommendations is conflicting or insufficient, requiring further study |
| ☒ | **Not recommended:** high level empirical evidence of no benefit or potential harm |

### Non-pharmacological interventions

A wide range of non-pharmacological approaches have been used to treat persistent and intractable hiccoughs; however, their safety and efficacy are unknown as no systematic reviews or clinical trials were found.[8,13] Most treatments have a physiological basis that interrupts the hiccough reflex arc by stimulation of the vagus or phrenic nerves to interfere with normal respiration, or increase pCO2 levels.[4]

#### Interventions available in the home and residential care facilities

- ⬟ **Breathe holding** or **drinking** in small sips.[8,13, 33]
- ⬟ **Sip** iced water or **swallow** crushed ice.[33]
- ⬟ **Breathe into a paper bag**, particularly if patient is hyperventilating.[33]
- ⬟ **Behavioral techniques** such as distraction, small meals, fasting and vigorous exercise (may not be an option in frail elderly or advanced disease patients).[9]

*Non-Pharmacological interventions continued on* next page

## Non-pharmacological interventions *continued*

**Rub** the soft palate (e.g., with a swab) to stimulate the nasopharynx.[33] Caution as this may trigger gag reflex.

### Interventions requiring additional equipment or admission to acute care

**Nebulized normal saline** — 2ml of NaCL 0.9% nebulized over 5 minutes at regular intervals throughout the day and prn at night. 43 Needs more study but safe; permits patient self-care and could be considered before drug treatment where equipment is available. **Note: in community, may be able to rent or borrow a home nebulizer machine.**

**Acupuncture**,[1,9,33] if available and acceptable to the patient.

**Surgical treatmen**t has shown benefit when cause is known and possibly removable. Cervical phrenic nerve block, only as last resort.[38] Careful patient selection required. Consider implications for overall quality of life. Rarely indicated in the frail elderly[9] or advanced disease patient.

## Pharmacological interventions

A systematic review found little high-level evidence for either non-pharmacological or pharmacological interventions that are effective or harmful.[25] Palliative experts lack consensus of medications considered essential for safe and effective hiccough management and acknowledge that additional research is needed.[44]

As hiccoughs often terminate spontaneously,[25,32,45] drug therapy usually is not indicated unless persistent.

Direct treatment to underlying cause of the condition whenever possible.[6,9,50,60] Baclofen and gabapentin have a lower risk of long term side effects than neuroleptic agents.[50] They are now preferred over chlorpromazine which can be poorly tolerated.[8,41,51]

### Baclofen

Supported by two small RCTs,[40,46] and several case reports .[38,40,46-48] It is suggested to have the best ability to treat hiccoughs.[1, 9] Has been used in cancer and palliative patients with success.[38,45,47,49]

*Pharmacological interventions continued on* next page

## Pharmacological interventions *continued*

- Single doses of baclofen 10 mg have successfully stopped hiccoughs after 0.5 to 3 hours.[47] This may provide immediate patient comfort if a diagnostic process takes several days.[47]
- Ongoing dosing of baclofen 10 mg bid, up to 10 mg TID, may be indicated for 2 to 5 days.[47]
- Use for a longer duration is indicated if unable to remove triggering cause.[47]

### Gabapentin

- May be preferred in hiccoughs related to CNS disease or if neuropathic pain coincides.[50,51] Has been shown to be effective with advanced cancer patients.[15]

### Adjunctive therapy

- Antiemetics may be required if vomiting accompanies hiccoughs.[4]
- Anxiolytics (e.g., midazolam) if hiccough distress is severe.[25,24] Consider in last days of life.

For more information, see Medications for Management of Hiccoughs.

## Patient and family education[1,8,20,32,33,41,42]

- Hiccoughs that last < 48 hours usually resolve on their own.
- Hiccoughs are often caused by gastric distention, carbonated beverages, alcohol, hot or cold drinks, anxiety or stress.
- Simple non-drug approaches may be helpful, especially if helped in the past.
- Draw from strategies identified in non-pharmacological interventions.
- Contact healthcare provider for hiccoughs that interfere with sleep, or > 2 days.

# ADDITIONAL RESOURCES FOR MANAGEMENT OF HICCOUGHS

## Resources specific to Hiccoughs

No additional resources specific to hiccoughs included in this document

## General Resources

- **Provincial Palliative Care Line** – for **physician** advice or support, call **1 877 711-5757** In ongoing partnership with the Doctors of BC, the toll-free Provincial Palliative Care Consultation Phone Line is staffed by Vancouver Home Hospice Palliative Care physicians 24 hours per day, 7 days per week to assist physicians in B.C. with advice about symptom management, psychosocial issues, or difficult end-of-life decision making.
- BC Centre for Palliative Care: Serious Illness Conversation Guide
  - ➡ http://www.bc-cpc.ca/cpc/
- BC Guidelines: Palliative Care for the Patient with Incurable Cancer or Advanced Disease
  - ➡ http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/palliative-care
- BC Palliative Care Benefits: Information for prescribers
  - ➡ http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/plan-p-bc-palliative-care-benefits-program
- National Centre for Complementary and Alternative Medicine (NCCAM) for additional information on the use of non-pharmacological interventions
  - ➡ https://nccih.nih.gov/
- Canadian Association of Psychosocial Oncology: Pan-Canadian Practice Guideline: Screening, Assessment and Management of Psychosocial Distress, Depression and Anxiety in Adults with Cancer
  - ➡ http://www.capo.ca/wp-content/uploads/2015/11/FINAL_Distress_Guideline1.pdf

*Additional resources for management of hiccoughs continued on* next page

## ADDITIONAL RESOURCES FOR MANAGEMENT OF HICCOUGHS *CONTINUED*

- Fraser Health psychosocial care guideline
  - ➞ https://www.fraserhealth.ca/media/psychosocial%20care.pdf

### Resources specific to health organization/region

- Fraser Health
  - ➞ http://www.fraserhealth.ca/health-professionals/professional-resources/hospice-palliative-care/
- First Nations Health Authority
  - ➞ http://www.fnha.ca/
- Interior Health
  - ➞ https://www.interiorhealth.ca/YourCare/PalliativeCare/Pages/default.aspx
- Island Health
  - ➞ http://www.viha.ca/pal_eol/
- Northern Health
  - ➞ https://www.northernhealth.ca/Professionals/PalliativeCareEndofLifeCare.aspx
- Providence Health
  - ➞ http://hpc.providencehealthcare.org/
- Vancouver Coastal Health
  - ➞ http://www.vch.ca/your-care/home-community-care/care-options/hospice-palliative-care

*Additional resources for management of hiccoughs continued on* next page

# ADDITIONAL RESOURCES FOR MANAGEMENT OF HICCOUGHS *CONTINUED*

## Resources specific to patient population

- ALS Society of Canada: A Guide to ALS patient care for primary care physicians
  - ➡ https://als.ca/wp-content/uploads/2017/02/A-Guide-to-ALS-Patient-Care-For-Primary-Care-Physicians-English.pdf
- ALS Society of British Columbia 1-800-708-3228
  - ➡ www.alsbc.ca
- BC Cancer Agency: Symptom management guidelines
  - ➡ http://www.bccancer.bc.ca/health-professionals/clinical-resources/nursing/symptom-management
- BC Renal Agency: Conservative care pathway and symptom management
  - ➡ http://www.bcrenalagency.ca/health-professionals/clinical-resources/palliative-care
- BC's Heart Failure Network: Clinical practice guidelines for heart failure symptom management
  - ➡ http://www.bcheartfailure.ca/for-bc-healthcare-providers/end-of-life-tools/
- Canuck Place Children's Hospice
  - ➡ https://www.canuckplace.org/resources/for-health-professionals/
    - 24 hr line – 1.877.882.2288
    - Page a Pediatric Palliative care physician – 1-604-875-2161 (request palliative physician on call)
- Together for short lives: Basic symptom control in pediatric palliative care
  - ➡ http://www.togetherforshortlives.org.uk/professionals/resources/2434_basic_symptom_control_in_paediatric_palliative_care_free_download

## UNDERLYING CAUSES OF HICCOUGHS IN PALLIATIVE CARE [2,5,7,8,38,45]

| Table 1 Drugs reported to cause hiccoughs | | | |
|---|---|---|---|
| Alcohol | Cyclophosphamide | Gemcitabine | Muscle relaxants |
| Anabolic steroids | Chorionic Gonadotropin | Heroin | Nicotine |
| Aprepitant | **Corticosteroids** | Hydrocodone | Paclitaxel |
| Aripiprazole | **Dexamethasone**** | Irinotecan | Perphenazine |
| Barbiturates | Donepezil | Levodopa | Pergolide |
| **Benzodiazepines** | Docetaxel | Macrolide antibiotics | Progesterone |
| Bupivacaine epidural | Doxycycline | Megestrol | Rocuronium |
| Carboplatin | Ethosuximide | Methotrexate | Sulfonamides |
| Cefotetan | Etomidate | Methylprednisolone | Triamcinolone |
| Chlordiazepoxide | Etoposide | Mexiletine | Vinorelbine |
| **Chemotherapy*** | Fluoroquinolone antibiotics | Midazolam | Zolpidem |
| Cisplatinum | Flumazenil | Morphine | |

* Chemotherapy may be falsely attributed as a cause because dexamethasone is often used concurrently.[52]

** May be dose-related; more prevalent at dexamethasone doses greater than 10 mg daily.[52]

## MEDICATIONS FOR MANAGEMENT OF HICCOUGHS

There are no approved medications for hiccough use in Canada; everything is off-label.

| Drug, Action | Dose, therapeutic range | Onset, Adverse Effects, Precautions and Dosing Concerns |
|---|---|---|
| Baclofen<br>1st line empiric[8,31,38,40,41,50,53,54] | 5 to 20 mg PO every 6 to 12 hour, up to 40 mg/day | Drowsiness, dizziness, hypotension, confusion, nausea, ataxia.<br>Alcohol and CNS depressants can be additionally sedating.<br>Avoid in renal failure, or carefully adjust dose due to risk of delirium, respiratory depression.<br>Risk of withdrawal symptoms when abruptly stopped.<br>Use caution in patients with epilepsy. |
| Gabapentin<br>1st line empiric[8,15,51,50] | 100 mg TID to QID to start then titrated up until results are seen, maximum 1200 mg/day | Drowsiness, dizziness, fatigue, ataxia, peripheral edema, visual disturbances, clumsiness/ unsteadiness. Adjust dose for reduced renal function.<br>No hiccough treatment studies in renal impairment.<br>In extended therapy, when possible, gradually reduce dose over a minimum of one week.<br>Very few drug interactions |

*Medications for management of hiccoughs continued on* next page

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## MEDICATIONS FOR MANAGEMENT OF HICCOUGHS *CONTINUED*

| | | |
|---|---|---|
| Metoclopramide<br>2nd line empiric [32,41,50,55,56] | 10 mg PO,IV,SC TID to QID | Asthenia, headache, drowsiness, fatigue. Serious: tardive dyskinesia, neuroleptic malignant syndrome.<br><br>Adjust dose for reduced renal function.<br>Avoid concurrent use with:<br>• Peppermint water (opposing actions on gastro-esophageal sphincter).<br>• Haloperidol due to increased risk of extrapyramidal symptoms.<br>• GI hemorrhage, mechanical obstruction, or perforation or if GI stimulation might be dangerous.<br>• Parkinson disease.<br>Use caution in patients with epilepsy.<br>Oral metoclopramide is 50-80% bioavailable, consider reducing SC, IV, IM dose by 25-50%. |
| Domperidone<br>2nd line empiric[2,32,50,55] | 10 mg TID to QID | Adverse effects; xerostomia, serious is prolonged QT interval, sudden cardiac death, ventricular arrhythmia. Risk of QT interval prolongation at doses greater than 30 mg/day. Check concurrent drugs for QTc risk. |
| Pantoprazole[41,57] | 40 mg daily to BID | Generally safe. Few drug interactions compared to other PPIs. Concomitant use of antacids does not affect the pharmacokinetics of pantoprazole sodium. |
| Antacid containing simethicone[32] | 10 mL QID | |
| Gaviscon [50] | 10 mL TID | Give after meals. |

## OTHER PROPOSED DRUG TREATMENTS

(Recommended Only After Palliative Care Consultation)

| Medication | Dose | Adverse Effects, Precautions and Dosing Concerns |
|---|---|---|
| Amantadine[58,59] | 100 mg PO once or twice daily | Non-sedating. Adjust dose for renal function.<br>Three cases (one was cancer/end of life). |
| Chlorpromazine[5,8,9,41,50-52,60,61] | 25 to 50 mg PO once daily, titrating up to 3 or 4 times daily | Hypotension, sedation, urinary retention, glaucoma, delirium, extrapyramidal symptoms.<br>Assess risk of QTc prolongation, often concerning.<br>Poorly tolerated in elderly patients.<br>Avoid long term due to risk of tardive dyskinesia. Injection discontinued, no longer available in Canada.<br>Only 25, 50 and 100 mg tablets available. |
| Dexamethasone[5,33,62] | 4 up to 8 mg PO daily | Fatigue, sleep disturbance, hiccoughs.<br>Suggested for hepatic or cerebral tumor – to reduce compression/irritation. Few studies. |
| Haloperidol[9,56,63] | 0.5 to 5 mg PO TID<br>Or via SC, IV, IM routes | Avoid concurrently with metoclopramide due to increased risk of extrapyramidal symptoms.<br>Recommended dosing from references varies widely.<br>Older studies used IM route, effectiveness via other routes uncertain, but much less painful.<br>Oral haloperidol is 60-70 % bioavailable, consider reducing SC, IV, IM dose by one-third. |

## OTHER PROPOSED DRUG TREATMENTS *CONTINUED*

(Recommended Only After Palliative Care Consultation)

| Medication | Dose | Adverse Effects, Precautions and Dosing Concerns |
|---|---|---|
| Lidocaine 2% viscous [55,64] | 5 mL orally BID to TID | Single case report. Was swallowed in 3 patients; 2 used with baclofen.<br>May impair swallowing, enhancing aspiration risk. Avoid food ingestion for 60 minutes. |
| Lidocaine[1,5,41] | 1 mg/kg loading dose followed by infusion of 2 mg/min CSCI | Risk of cardiovascular and neurologic toxicities. |
| Methotrimeprazine[32] | 3 to 6 mg PO,SC,IV HS | Injectable alternative to chlorpromazine or haloperidol |
| Midazolam [5,24,33,56] | 5 to 10 mg SC or PO Q4H PRN CSCI: 10 up to 120 mg/day | Two case reports. Review use and suitability with local palliative care team.<br>Adverse effects include sedation, risk of apnea paradoxical reactions, drug interactions, especially with opioids.<br>reduced elimination in liver or heart failure, and elderly |
| Olanzapine [60,65,66] | 2.5 to 7.5 mg PO daily | Three cases reports. In two, used in combination with baclofen as 5 mg baclofen BID, other 10 mg TID. |
| Pregabalin [50,67,68,69] | 25 to 75 mg PO BID, up to 375 mg/day | Drowsiness (might be less than gabapentin), dizziness, peripheral edema. Three case reports. |
| Sertraline [70] | 50 to 150 mg PO/day | Single patient case report. |
| Valproic acid [5,50] | 15 to 20 mg PO per kg/24 hours, divided in 1 or 3 doses | May increase by 250 mg/week until hiccoughs stop. |

*Other proposed drug treatments continued on* next page

## OTHER PROPOSED DRUG TREATMENTS *CONTINUED*

(Recommended Only After Palliative Care Consultation)

† Off-label. PO = by mouth IV = Intravenous, SC = Subcutaneous, TID = three times daily, QID = four times daily ODT = oral dissolving tablet, CSCI = continuous subcutaneous infusion.

Prices for prescription drugs may be obtained from BC PharmaCare. The British Columbia Palliative Care Benefits Plan (http://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/palliative-formulary.pdf) provides province-wide drug coverage for many of the recommended medications; check website to confirm coverage. Consider price when choosing similarly beneficial medications, especially when the patient/family is covering the cost.

## HICCOUGH MANAGEMENT ALGORITHM

No management algorithm included in this document.

## HICCOUGH EXTRA RESOURCES OR ASSESSMENT TOOLS

No extra resources or assessment tools included in this document.

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